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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,464	04/29/2002	Peter L. Oren	29342/36230A	6930

4743 7590 06/02/2004

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,464	OREN ET AL.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-24-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of IDS dated 6-24-02 is acknowledged.

Claim 27 has been canceled and claims 1-26 are pending in the instant application.

Claims 1is directed to a pharmaceutical composition comprising a beta-carboline (formula I) as a free drug, a diluent, a lubricant, disintegrant and a binder. Claims 2-16 & 19 dependent from claim 1 recite the specific excipients and percentages of the excipients. Dependent claim 17 recites that drug is provided as particles and 90% of the particles have a size less than 40 microns. Claim 18 recites particle size as less than 10 microns. Claims 20-21 depend from claim 18. Claims 22-24 recite a tablet comprising composition of claim 1 and, claim 25 recites a capsule comprising composition of claim 1. Claim 26 is directed to a method of treating a patient in need thereof with the composition of any one of claims 1-21.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9, 11-16 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/03675 (Daugan).

Daugan discloses the claimed beta-carboline compounds and compositions containing the compounds, as also acknowledged by applicants on page 2 of the instant application. Daugan specifically discloses instant preferred compound (instant specification, page 3, lines 28-30) for treating conditions where inhibition of PDE5 is beneficial (see page 3, lines 24-25, lines 30-32 and is also referred to as compound A). On page 12, lines 11-12, Daugan discloses that the compounds a and B are prepared as different dosage forms and in particular, Table B shows a tablet prepared by wet granulation, where in the tablet composition contains beta-carboline drug as active agent and other excipients such as polyvinylpyrrolidone, PEG, Polysorbate 80, magnesium stearate, crosscaramellose sodium, and microcrystalline cellulose, which read on the instant claimed binder, diluent, wetting agent, lubricant and disintegrant respectively. Instant dependent claims specifically recite the excipients of Table B of Daugan. With respect to the percentages of active ingredients and the excipients claimed, the total weight of the composition of tablet in Table B is 500 mg. A calculation of the proportion of each ingredient in Table 2 reads on the instant claimed percentages. With respect to the claimed "free drug", Daugan does not teach an intimately embedded drug in a polymeric co-precipitate and hence meets the definition of instant "free drug" (instant page 5, lines 24-27). Instead, Daugan only discloses direct compression or wet granulation followed by compression to prepare the tablets (pages 12-14). Accordingly, Daugan anticipates instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 8, 10, 19 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03675 (Daugan).

Daugan, discussed above, fails to teach the exact or the percentages of diluent (claim 5), lubricant (claim 8), binder (claim 10), and the claimed amounts of drug in tablet (claims 22, 23) and capsule (claim 25). However as acknowledged by applicants, Daugan teaches the active agent and also for the same purposes i.e., as a 5PDE inhibitor. Further Daugan teaches the same pharmaceutical compositions containing the same active compound and excipients, as claimed, in the form of tablets and capsules. Accordingly, optimizing the amounts of art recognized excipients such as binder, lubricant, optimizing the amount of active compound with an expectation to achieve the appropriate dosage form as well the desired therapeutic efficiency of the drug would have been within the scope of a skilled artisan because Daung suggests optimizing the amounts of drug in the range of 0.5 to 800 mg per day and also employing the suitable excipients depending on the route of administration (page 5).

Claims 17, 18, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03675 (Daung) as applied to claims 1-16, 19, 22-26 above, and further in view of WO 96/38131 (Butler) and US 4,721,709 to Seth et al (Seth).

Instant claims recite particulate drug and in particular, where at least 90% of the particles have a size of less than 40 microns (claim 17) or less than 10 microns (claim 18). Daung fails to teach drug particles, as claimed.

Butler teaches pharmaceutical compositions comprising beta-carboline compounds (abstract, page 4, lines 15-21). The specific beta-carboline compound taught by Butler is the same as that claimed in the instant invention. Further, Butler teaches that the above are poorly soluble in nature. Butler teaches solid dispersions but fails to teach the claimed particle sizes.

Seth teaches pharmaceutical composition containing poorly water-soluble drugs and a method of preparing the same. The method of Seth is practically applicable to all water insoluble drugs and comprises the steps of providing dry powder of the insoluble drug that is adsorbed on to a carrier such as starch or cellulose and is characterized in that the drug is present particulate form and at least 95% of the drug particles have a mean size of less than 15 microns (col. 4, lines 44-53, col. 3, lines 60-67), which is in the same range as claimed. Seth teaches that the drug particles are closely associated with the carrier and details the method of preparing the formulation in col. 6, lines 1-39. Further, Seth teaches preparation of various dosage forms such as tablets, capsules etc., with the above prepared formulation (col. 8). Examiner notes that instant specification refers to US patent 4,605,517 by incorporation for the preparation of the instant drug formulation. It is noted that the above patent also recites the same method of preparation as that of Seth. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare drug formulations of beta-carboline of Daugan containing the excipients such as lubricants, wetting agents etc., by the process of Seth i.e., particulate drug adsorbed on to excipients or carrier and compressing into tablets because Seth teaches that the

conventional methods of jet milling or pin milling employed in drug preparation result in slow dissolution and absorption, (col. 2, lines 1-20) and that their method avoids the disadvantages of agglomeration and poor flow seen in the conventional methods. Accordingly, the expected result would be an increased dissolution of beta-carboline and hence increased bioavailability without agglomeration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 8, 9, 12-21 and 22-24 of copending Application No. 10/031,531and over claims 1-9 and14-16 of copending Application No. 10/031,463. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claimed composition containing a free drug, beta-carboline together with excipients and also composition comprising particulate form of the drug is also claimed in the above patent applications. US application 10/031,531 the composition

of the instant claims in the form of capsules, which is reads on the claimed subject matter of instant claim 25. Further, method of treating specific disorders using the above composition by '131 anticipates instant method of treatment. Accordingly, claims of application 10/031,531 anticipate instant claims.

US application 10/031,463 claims a free drug particulate form of beta-carboline, compositions containing the free drug, a method of treating a patient in need thereof. The copending claims also recite particle sizes, carriers or excipients, which read on the instant dependent claims. Accordingly, the copending claims directed specifically to particulate beta-carboline compound, composition containing particulate compound anticipate instant broadly recited pharmaceutical compositions and method claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-26 are directed to an invention not patentably distinct from claims 1, 4, 8, 9, 12-21 and 22-24 of commonly assigned 10/031,531. Specifically, the copending application describes pharmaceutical compositions containing the same drug, i.e., beta-carboline compounds, in the form of free drug and also in particulate form and for the treatment of the same disease or disorders, also described in the instant application.

Claims 1-26 are directed to an invention not patentably distinct from claims 1-9 and14-16 of commonly assigned Application No. 10/031,463. Specifically, the copending application describes pharmaceutical compositions containing the same drug, i.e., beta-carboline

compounds, in the form of free drug and also in particulate form and for the treatment of the same disease or disorders, also described in the instant application.

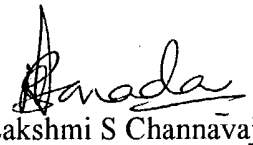
The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/031,151 and 10/031,463, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615
May 29, 2004